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EDITORIAL

NEW TREATMENTS

VETERINARY medicine, like human medicine, makes full use of the results of research work in the treatment and control of disease. Old, and sometimes well-established, methods give place to recently-introduced techniques, proved valuable by laboratory experiments and field trials. One of the outstanding advances is the introduction of new chemo-therapeutic agents. The use of drugs of the sulphonamide series can now be considered as established: the application of antibiotics in disease control is now an everyday occurrence. The search for new chemical agents continues, and as they are discovered, and the results of their trials become available, they become part of the general stock of drugs recommended and used by the veterinary profession in their everyday work.

In the control of bovine mastitis, sulphanilamide was introduced and proved of considerable value. With the discovery of penicillin as an agent lethal to various micro-organisms, including streptococci, the control of one of the commonest forms of mastitis became a practical proposition. It is to be hoped that further discoveries will lead to the control of forms of mastitis which are still resisting the treatments which are available to-day.

The use of drugs of the sulphonamide series in the control of coccidiosis of chicks must be regarded as a stage of momentous importance in the control of that infestation. It completely altered our methods of controlling the disease and gave us a technique not only for cutting short an infection which caused heavy losses, but, when properly applied, did not interfere with the immunity associated with a natural attack of the disease. Poultry-keepers have derived

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much benefit from the research work of Taylor and Horton-Smith in this country. As was to be expected, when new chemo-therapeutic agents became available their value in controlling coccidiosis had to be tested, and in this issue of the BRITISH VETERINARY JOURNAL we publish the results of the investigations of Horton-Smith on the use of nitrofurazone. It will be seen from the article that this recently-introduced drug can be used effectively in the control of cæcal coccidiosis. It conforms with the requirements demanded of a suitable drug in that in low dosage it is coccidiostatic, prevents infestation, and its use "permits the normal development of immunity to cæcal coccidiosis in chicks exposed to infections of *Eimeria tenella* during treatment." Without doubt, as research work continues, drugs will be found to assist us in the combating of coccidiosis associated with the presence of other coccidia.

In the past we have been apt to stress the importance of controlling disease by the induction of immunity by the use of vaccines and serums. Such products have been, and still are, of immense value. The introduction of chemo-therapeutic agents, however, is gradually paving the way for new lines of treatment: sometimes when used alone, or at other times when coupled with the use of serum, they are proving their value in disease control. Research into the development of such agents for our work must continue to be encouraged, and our methods of disease control will surely be governed by the discovery of new agents specific for their action on individual or groups of micro-organisms.

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GENERAL ARTICLES

STUDIES IN BOVINE MALIGNANT CATARRH
1. Experimental Infection in Cattle

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Introduction

Bovine malignant catarrh has been recognised in Africa since very early times. Thus, Mettam (1923), studying the disease in South Africa, quotes Cumming as writing, in 1850, " of the danger of the oxen taking a horrible fatal illness, called by the Boers snotsickness, which cattle are very liable to get from pasturing on ground frequented by black wildebeeste." It is interesting to note that the role played by wildebeeste in the transmission of African malignant catarrh was already suspected. In Europe, too, the disease has been known for over a century. It was not until comparatively recent times, however, that Mettam (1923) and Götze and Leiss (1929) first transmitted malignant catarrh to cattle by the inoculation of infective blood. Reports of experimental studies published during and immediately after this period are characterised by somewhat conflicting views. Mettam (1923), for example, considered that South African "Snotsiekte" was essentially a different disease from European malignant catarrh, view which has subsequently been disproved (Daubney and Hudson, 1936; de Kock and Neitz, 1950). Successful transmission to cattle by blood inoculation was achieved by Mettam (1923), Götze and Leiss (1929), and Rinjard (1935), whereas Dobberstein and Hemmert-Halswick (1928), Stolnikof (1933), and de Kock and Neitz (1950) failed to do so. The inability to infect cattle with filtered material, or to transmit the disease by direct contact was consistently reported, with the exception of Zanzucchi (1934), who claimed success by both methods. Götze (1930) found that infective blood became inocuous within 24 hours, whereas Mettam (1923) was able to infect cattle with refrigerated blood stored for 11 days. Confusion also existed as to the ætiological relationship between malignant catarrh and Borna disease of horses (Ernst and Hahn, 1927; Zwick and Witte, 1931).

Most European workers, however, accepted the view that sheep played an important part in the maintenance and spread of the disease. Götze (1930) presented impressive evidence in favour of this hypothesis when he obtained sheep from an infected farm and placed them in contact with susceptible cattle. Of the 50 animals thus exposed, 94 per cent developed malignant catarrh. In South Africa, Mettam (1923) failed to infect sheep, but proved that wildebeeste may act as carriers when he reproduced malignant catarrh in cattle with blood obtained from an apparently healthy wildebeeste. Daubney (1939) stated: " Further work on this disease has failed to demonstrate any connection between sheep and the infection in bovines."

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In 1936, Daubney and Hudson opened up new possibilities for experimental study by publishing an account of successful transmission experiments using a strain of the "head and eye" form (Götze, 1930) of the disease. They were able to infect 33 cattle through four serial passages by the subcutaneous inoculation of large quantities of defibrinated blood, and by the intraglandular inoculation of brain or lymphatic gland suspensions. They also established their strain in rabbits, using the intracerebral route, and subsequently reproduced malignant catarrh in cattle by the intraglandular inoculation of third passage rabbit brain.

Little further experimental work appears to have been done on malignant catarrh, apart from that of Pattison (1946), who was able to infect one generation of rabbits with a strain of malignant catarrh isolated in Palestine, and de Kock and Neitz (1950), who confirmed Götze's (1930) observations by reproducing malignant catarrh in cattle placed in close contact with sheep obtained from an infected farm.

In Kenya, the incidence of malignant catarrh is considered to be comparatively low, but there is good reason to suspect that many cases are unrecognised, or confused with other diseases, such as East Coast fever, rinderpest and bacillary necrosis. The incidence may, therefore, be much higher than is commonly supposed. Departmental files first record the existence of this disease in 1934, and since then sporadic outbreaks have been reported from time to time from widely separated districts, such as Nanyuki, Njoro, Kajiado, Machakos, Athi River, Nairobi, Ngong, Garissa, Nakuru, Maralal, Samburu, Makuyu, Konza, Maseno and Kitale. The disease is also enzootic in certain parts of the Masai native reserve, where wildebeeste are commonly considered to harbour the virus, and little or no estimate can be made of the annual losses that occur amongst the nomadic cattle of those areas.

Malignant catarrh in this Colony usually conforms close with Götze's (1930) description of the "head and eye" form of the disease. In addition, Daubney (1934) has described a very mild form which might easily pass unrecognised. Mortality in the "head and eye" form is usually very high, approaching 100 per cent, and the appearance of the disease amongst the high-grade and pure-bred exotic breeds of cattle, now commonly found in the European farming areas, presents grave problems to the Veterinary Department and the stock-owner alike. Since no methods of prevention or treatment are known, losses amongst these valuable cattle may reach very serious economic proportions.

At the Ngong African Veterinary Training Centre, situated near Nairobi, the "head and eye" form of malignant catarrh has been enzootic for many years. A valuable pure-bred herd of a selected strain of Zebu cattle has gradually been established, but losses through this disease have at times imperilled the whole project. Deaths from malignant catarrh have occurred sporadically over the past 15 years, reaching a peak in 1949 and 1950, when 72 animals were lost during a period of 18 months. This caused considerable financial loss and gross interference with the breeding scheme.

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The disease at Ngong was particularly virulent in character and affected animals invariably died. Two separate herds of cattle were maintained, a dairy herd which was confined at night within the farm buildings and in close proximity to a flock of some 200 head of Red Masai sheep, and a ranch herd which was maintained on another part of the farm. It was in the dairy herd that malignant catarrh occurred, cases in the ranched herd being very rare. The most susceptible age appeared to be between eight and 18 months, that is, during the weaning period, but fatalities also took place from time to time in animals of all ages. The disease was typically the "head and eye" form, characterised by a high temperature, profuse ocular and nasal discharges, swollen glands, rapid emaciation, and death.

In 1949, it was decided to attempt to establish the Ngong strain of virus in cattle and small animals at the Kabete laboratories as a preliminary to further investigations into the nature and behaviour of the organism.

Experimental

(i) *Infection of Cattle.*

On October 9, 1949, a native cow, showing classical symptoms of "head and eye" malignant catarrh, was received from Ngong. It was destroyed and a 20 per cent suspension of its prescapular lymph gland prepared, using its own defibrinated blood as a diluent.—10 c.c. of this mixture was immediately inoculated into the left prescapular gland of bovine 7872. This animal remained healthy over a period of several months.

A month later, another cow in the advanced stages of malignant catarrh was received. In addition to the usual symptoms this animal was suffering from a peeling of the skin inside the axillæ, on the udder and teats, and on the left side of the chest. The following day this animal was destroyed *in extremis* and gland and citrated blood stored overnight at —30 degrees C. The material was then thawed and a 20 per cent suspension of gland prepared, using the citrated blood as a diluent. This was inoculated to rabbits and mice by the intracerebral route. The animals remained healthy over a two months' period of observation.

Some weeks later a further typical case in a young Zebu bull was received. This animal died early one morning. When opened, the carcass was still warm and blood ran freely. A mixture of sub-maxillary lymph gland and citrated blood was prepared and inoculated immediately into mice, rabbits and guinea-pigs, all by the intracerebral route. Nine-day-old embryonated eggs were also inoculated on to the chorio-allantois. Finally, 10 c.c. of a mixture of brain, gland and citrated blood was inoculated into the right prescapular gland of a grade steer, number 8766.

The inoculated guinea-pigs died overnight as a result of traumatic damage. One of the rabbits commenced to show nervous symptoms 20 days after inoculation, and died suddenly two days later. A portion of its brain was sub-inoculated into two other rabbits intracerebrally without, however, causing any signs of ill-health over a period of two months. Of the mice, about 20 per cent

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showed evidence of hypersensitivity after one month, but further sub-inoculations failed to reproduce these symptoms. Bovine 8766 remained healthy. In the inoculated eggs a noticeable thickening and œdema of the chorio-allantois membranes occurred, but bacterial contamination nullified subsequent sub-inoculations.

Three more cases from Ngong were investigated in a similar manner with unfruitful results. At about the same time cases of a similar type of malignant catarrh from Makuyu (40 miles North-East of Nairobi) and Konza (50 miles South-East of Nairobi) were received, but attempts to establish these strains in laboratory animals were unsuccessful. The Konza strain was also given to mice by inhalation in the hope that the virus might exhibit pneumotropic properties. Mice were sacrificed weekly and suspensions of lung given to fresh series of mice by inhalation. For a time it seemed as if constant pneumonic lesions were developing. For example, five out of nine lungs from third generation mice showed marked lobar pneumonia with patches of consolidation. When these nine lungs were checked for freedom from bacteria, seven of them proved to be sterile. Unfortunately, this series had to be discontinued owing to an outbreak of salmonellosis.

Whilst these investigations were proceeding, a severe outbreak of the " head and eye " form of malignant catarrh occurred on Mr. " D.'s " farm, which is situated on the Athi Plains, a few miles East of Nairobi and contiguous with the Royal National Park. Contact between the cattle concerned and wildebeeste, which at this time were calving, was not unusual. Since the stock consisted mainly of high-yielding Fresian cows, the owner was faced with the probability of a severe economic loss. A post-mortem examination on one of the early cases confirmed the identity of the disease, and the next day a visit was paid to the farm, when four more typical cases were observed. In all, 24 animals were lost.

In an effort to stem the spread of the disease, it was decided to inoculate the whole herd with a formalinised vaccine, using material obtained from an animal in the advanced stages of the disease. This was done, with apparently successful results (Piercy, 1951*b*). The technique adopted followed closely the method used at this laboratory for the production of rinderpest inactivated spleen vaccine. The material is minced, suspended in 9 per cent saline, and stored overnight at ±4 degrees C. The next morning sufficient distilled water is added to adjust the salt to 0.9 per cent, and after thorough shaking for one hour, the mixture is screened through muslin and formalinised.

This procedure was carried out, using a mixture of spleen, brain, kidney and gland. Before adding the formalin, however, a portion of the mixture was removed and inoculated into two laboratory animals, as follows: Bovine 9622 received 10.0 c.c. into the left prescapular gland, and bovine 9629 10.0 c.c. intravenously. Twenty-seven days later, bovine 9622 reacted and developed typical malignant catarrh. It was destroyed *in extremis* a week later, and the post-mortem findings confirmed the diagnosis of malignant catarrh. All subsequent virus passages stemmed from this animal. Bovine 9629, inoculated

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intravenously, did not react and was subsequently shown to be susceptible by challenge.

The first needle passage having been successfully achieved, no further difficulty was encountered in maintaining infection by gland to gland inoculation. At the time of writing, the " D " strain is in its nineteenth bovine passage, involving 41 animals. Only one animal, a Boran steer (No. 1223) failed to react, and it was later shown to be susceptible. It may well have been that in this case the inoculum was accidentally deposited into extra-glandular tissues.

(ii) *Susceptibility.*

The total number of animals successfully infected during these investigations now exceeds 100. Considerable information has thus been acquired as to the relative susceptibility of animals of various ages and breeds. Pure-bred Zebu, low-grade, high-grade and pure-bred exotic breeds have all proved susceptible. Nor does age appear to qualify susceptibility, since both calves and adults have been infected without difficulty. This is supported by a remarkable instance at Ngong Veterinary Training Centre, where a 16-year-old Zebu cow and its unweaned calf both developed malignant catarrh at one and the same time.

(iii) *Incubation Periods.*

Table I gives the history of routine passages. Contrary to expectation, the average incubation periods showed little tendency to become shortened, and varied from 14 to 37 days, with an over-all average of 22.3 days. Even in the later passages considerable variation occurred between animals receiving the same inoculum. If a constant incubation period is considered as a prerequisite of " fixation," it cannot yet be said that the " D " strain has been " fixed." There may, however, be reasons associated with the mode of invasion, to be discussed later, why a fairly wide variation in incubation period must always be expected.

These results are in accordance with those of Mettam (1923), who noted incubation periods varying from 10 to 34 days, with an average of 21 days, and Daubney and Hudson (1936), in whose experiments there was a maximum of 60, a minimum of 14, and an average of 20.9 days. Götze (1930) records incubation periods as long as 10 months, but the strain he used was of European origin, which might well exhibit differences from African strains.

TABLE I

History of routine gland to gland passages of the " D " strain of malignant catarrh virus in cattle.

Generation.	Donor.	Animal.	Inoculum 10% gland.	Incubation periods. Days.	Mean.	Remarks.
1	" D " cow	9622	10.0 c.c.	22	22	
2	9622	62	1.0 c.c.	29		
	,,	25	5.0 c.c.	25		
	,,	9629	5.0 c.c.	31	28	
3	25	9153	2.0 c.c.	20		
	62	360	2.5 c.c.	23	21.5	

Generation.	Donor.	Animal.	Inoculum 10% gland.	Incubation periods. Days.	Mean.	Remarks.
4	360	579	2.0 c.c.	20		
	9153	60	2.0 c.c.	24	22	
5	60	352	2.0 c.c.	19		
	„	347	1.5 c.c.	23	21	
6	352	9608	2.0 c.c.	22		
	347	890	2.0 c.c.	19	20.5	Diphasic temperature rise with prolonged clinical reaction.
7	9608	1055	2.0 c.c.	17		No temperature reaction; sudden death.
	„	1053	2.0 c.c.	17		
	„	1012	2.0 c.c.	17		
	„	1048	2.0 c.c.	17	17	
8	1048	804	1.0 c.c.	28	28	Previously failed to react to gland diluted 1 : 100.
9	804	1016	2.0 c.c.	18		Mild temperature reaction (under 104 degrees C.).
	„	1190	2.0 c.c.	19	18.5	Mild temperature reaction (under 104 degrees C.).
10	1016	1217	2.0 c.c.	18	18	Previously failed to react to adrenal gland inoculation.
11	1217	1560	2.0 c.c.	21		
	„	1558	2.0 c.c.	23		
	„	953	2.0 c.c.	24	22.6	Previously failed to react to rabbit strain.
12	953	1635	2.0 c.c.	17		
	„	1634	2.0 c.c.	36		
	„	9130	2.0 c.c.	21	24.6	Mild temperature reaction (under 105 degrees C.).
13	9130	1740	2.0 c.c.	22		
	„	1724	2.0 c.c.	14	18	
14	1724	1898	2.5 c.c.	18		
	„	1900	2.5 c.c.	28	23	
15	1898	1999	1.5 c.c.	19		
	„	1830	1.5 c.c.	18	18.5	
16	1999	2061	2.5 c.c.	18		
	„	1980	2.5 c.c.	31	24.5	
17	2061	2171	2.0 c.c.	37		Recovered. Not yet challenged.
	„	1973	0.05 c.c.*	33	33	
	1980	2211	2.0 c.c.	—		Died suddenly from other causes.
18	1973	1894	2.0 c.c.	18		
	„	1893	2.0 c.c.	27	22.5	
19	1894	2376	2.0 c.c.			
	„	2470	2.0 c.c.			

* Note.—Bovine 1973, given 0.05 c.c. of white blood cells (Piercy, 1951a), was used to continue the routine passage series since bovine 2211 died of other causes and bovine 2171 recovered.

(iv) *Titration of Infective Gland.*

A 10 per cent suspension of sixth passage gland, taken from bovine 347 when reacting to malignant catarrh, was prepared. From this dilutions of 1 : 100 and 1 : 1,000 were made.—2.0 c.c. of each preparation were inoculated into the prescapular glands of three animals. Bovine 890 received the undiluted suspansion and bovines 804 and 815 the 1 : 100 and 1 : 1,000 dilutions respectively. All inoculations were made on the same day as the material was harvested. Bovine 890 died of malignant catarrh after 31 days, but neither of the two animals receiving diluted gland reacted. Bovine 804 (1 : 100 dilution) was shown to be fully susceptible by challenge, but bovine 815 (1 : 1,000 dilution) died suddenly from hoven 19 days after the challenge inoculation.

This experiment shows that the titre of available virus in a 10 per cent suspension of lymph-gland, as judged by the intraglandular inoculation of susceptible cattle, is very low, and may be less than 100 M.L.D.

(v) *Filtration Experiments.*

Gland removed from bovine 25, reacting to experimentally induced malignant catarrh, was frozen for two hours at —30 degrees C., rapidly thawed, ground up in a mortar with the aid of sterile sand and saline, and passed through a seitz E.K. filter pad under negative pressure. 2.0 c.c. of the filtrate was inoculated into the prescapular gland of bovine 257. A portion of unfiltered gland was given to bovine 9153. Bovine 257 did not react and was subsequently shown to be susceptible. Bovine 9153, receiving unfiltered gland, died of malignant catarrh 25 days after inoculation.

Using gland from bovine 9153, a second attempt was made to filter the virus. On this occasion the material was maintained overnight in a deep-freeze machine at —30 degrees C., thawed out the next morning, minced, equal parts of saline added, and the mixture shaken violently with beads for 30 minutes. The mixture was then filtered as before and 2.0 c.c. of the filtrate inoculated to bovine 61. A portion of the unfiltered material was given to bovine 60, which died of malignant catarrh 31 days later. The animal receiving filtered gland did not react and was later shown to be susceptible.

(vi) *Clinical Symptoms.*

These have been described in considerable detail by both Mettam (1923) and Daubney and Hudson (1936), whose findings agree with the author's own observations. Attention is drawn, however, to certain additional features peculiar to the present series.

The variation in incubation period has already been mentioned. Considerable variation was also noted in the clinical symptoms exhibited by individual animals. Thus, the profuse, ropey, yellow, muco-purulent nasal discharge so characteristic of natural infection disappeared in later passages and was replaced by a slight greyish discharge, more mucoid than purulent in nature. On the other hand, a watery, ocular discharge from one or both eyes, followed by a progressive corneal opacity, became a constant feature. Nervous symptoms occurred in a few animals and was usually characterised by a twitching of the

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eye-lids and ears. In some cases clinical symptoms were accompanied by mild febrile reactions only, the temperature remaining below 104 degrees C., whilst in others sudden death occurred. In one animal the temperature remained within the normal range throughout an otherwise characteristic fatal clinical reaction. In another, a protracted reaction was characterised by a diphasic temperature elevation (Figs. 1-4).

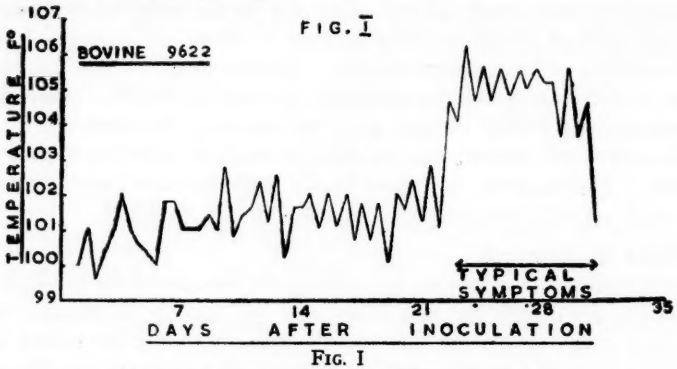

FIG. I
Malignant catarrh. Typical temperature reaction.

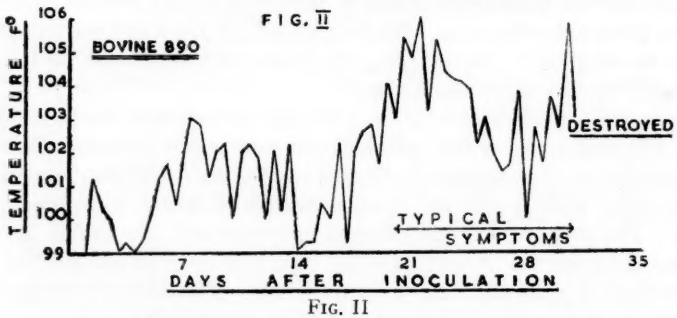

FIG. II
Malignant catarrh. Extended, diphasic temperature reaction.

(vii) *Post-mortem Lesions.*

In later passages, a tendency for the "D" virus to cause gastrotropic and enterotropic lesions was observed, hyperæmia and hæmorrhages in the abomasum, duodenum, cæcum and rectum being not uncommon. A striking lesion on the folds, and occasionally in the fundus of the abomasum, not previously described, was seen in a number of cases. This took the form of small, round, white foci, about 2 mm. in diameter, slightly raised above the surface of the mucous membrane, and with distinct black, crater-like depressions in the centre.

In a fairly extensive experience of post-mortem examinations this lesion has never before been encountered, and it is considered that it may be regarded as pathognomonic of malignant catarrh. The "complete peppering of the mucous membrane of the abomasum with pin-point and lenticular hæmorrhages,"

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described by Daubney and Hudson (1936) as a common feature, was seldom observed. The glands were hæmorrhagic in only about 20 per cent of cases, and their cut surfaces more usually presented a pale, white, granular appearance. Enlargement of lymph-glands, which was a constant feature, appeared to be due to proliferative changes rather than to œdema.

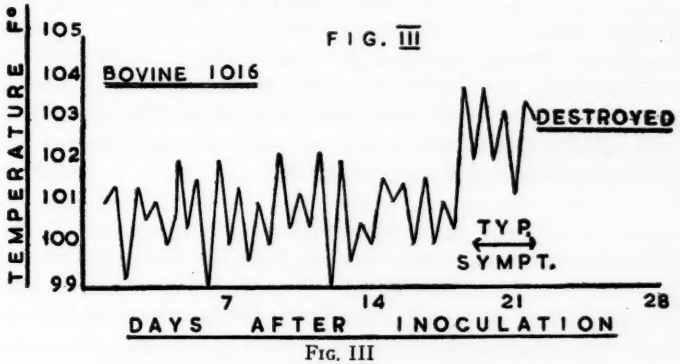

FIG. III

Malignant catarrh. Mild temperature reaction.

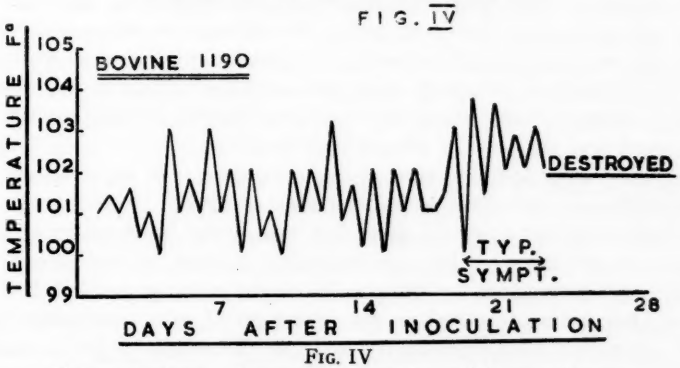

FIG. IV

Malignant catarrh. Temperature remaining within normal range.

Another very characteristic lesion was an erosion of the tips of the cheek papillæ, frequently accompanied by a pink discoloration. In nearly every case the lungs appeared to be normal macroscopically. Some œdema anteriorly was not uncommon, but pneumonic changes were extremely rare. This fact, which has been noted by other workers, is rather remarkable, considering the serious lesions, complicated by secondary bacterial invasion, commonly found in the pharynx, larynx and anterior air passages.

(viii) *Contact Infection.*

Instances of contact infection under experimental conditions are extremely rare. Daubney and Hudson (1936) were successful in infecting one calf by placing it in close contact with several other animals in the clinical stages of the

disease. Neither Mettam (1923) in South Africa nor Götze and Leiss (1929) in Europe were able to achieve contact infection. Zanzucchi (1934) recorded successful contact transmission from sheep to sheep, sheep to goats, and sheep and goats to bovines. A close study of this author's work, however, suggests that the disease concerned may not have been malignant catarrh as understood in Africa.

At Kabete, over 100 animals have reacted to and died from experimentally induced malignant catarrh during a period of some 18 months. Susceptible cattle have frequently lived in the same stall as reacting animals without contracting the disease, and at all times there have been other susceptible cattle in the same building and separated only by low, stone partitions. Yet not a single case of spontaneous infection has occurred.

Discussion

A point of interest is the ease with which the " D " strain of virus was transmitted to bovines in contra-distinction to repeated failures with material from three other outbreaks. The " D " and Ngong farms, separated only by some 10 miles, are similarly situated as regards climate and rainfall. The symptoms and lesions in cattle from these two outbreaks were macroscopically indistinguishable. It would, in fact, have been reasonable to suppose that the same strain of virus was responsible for them both. Nevertheless, it seems probable that this was not so, and that the behaviour of one strain of virulent virus, when subjected to certain experimental conditions, may be contrary to the behaviour of another, however closely allied they may be as judged by their environmental circumstances and the type of disease they produce.

The " D " virus has now been passaged 19 times, but no reduction in the average length of incubation period has been observed. The shortest period recorded was in bovine 1724 (14 days), but even in the latest passages considerable variation still occurred between individual animals treated in exactly the same way. An explanation for this may be sought in the probable behaviour of the virus after being deposited in the lymph-gland of a susceptible animal. There is substantial histo-pathological evidence (Plowright, 1951) to show that the predilection site for this virus is lymphoid tissue. When virus is injected into a lymph-gland, an initial resistance is encountered, characterised by an observable local reaction, after which it is possible that a gradual invasion of the lymphatic system occurs. When the lymphatic system as a whole becomes saturated, it may be that there is an overflow of virus into the blood stream, followed by the invasion of potentially lymphopoietic tissues, such as are found in sub-epithelial situations, together with a febrile reaction and the appearance of clinical symptoms. If the virus was absorbed into the blood stream in the first instance, and disseminated through the tissues, a shorter and more constant incubation period might be expected. This hypothesis is supported by the fact that in recent successful transmissions by the intravenous route (Piercy, 1951*a*), incubation periods have not been reduced, suggesting that even when virus is introduced directly into the blood stream it attacks the lymphoid system before

invading the tissues generally. An analagous predilection for specialised tissues is seen with rabies virus, which requires nervous tissue for its propagation. Here, too, owing to the route of invasion, the incubation period is lengthy and variable.

A peculiar feature of malignant catarrh is its comparatively low incidence, not only in susceptible cattle as a whole, but in a particular herd. Thus, although mortality may approach 100 per cent, many animals apparently escape infection. That this is not due to an individual resistance is suggested by the regularity with which animals have been infected in the present series. The method by which animals become infected in nature is, of course, still entirely unknown, but there are good grounds for believing that transmission is effected by a blood-sucking insect. If this be so, and if the hypothesis that initial multiplication will only take place in lymphocytic and lymphopoietic tissues be correct, an explanation becomes available for the low incidence of the disease and its lengthy and variable incubation period. The assumption would be that the majority of animals in a herd are attacked by infective vectors, but that in only a few instances is the virus deposited in tissues suitable for its continued existence and propagation. Furthermore, it could then be argued that other animals gain immunity through contact with virus which fails to overcome the body's resistance, and that, so long as infection remains enzootic, the resistance of such animals is constantly reinforced. It has already been stated that age in itself does not appear to qualify susceptibility, yet it is noteworthy that the majority of cases at the Ngong Veterinary Training Centre occurred amongst weaner stock. This suggests that the older animals were, in fact, relatively resistant as a result of constant exposure to the disease.

That no cases of spontaneous infection occurred amongst animals at the laboratory in contact from time to time with over 100 reacting animals, lends support to the theory held by some, for example, Miessner and Schoop (1934), that direct bovine transmission does not occur in nature, and that the presence of intermediate hosts, such as sheep, wildebeeste or other animals, is necessary for the spread of the disease. In this connection it is of interest to note that Daubney (1943) reports that Hudson successfully infected an African buffalo with a laboratory strain of malignant catarrh. During the experiments reported in this paper, sheep were at all times closely adjacent to or in the immediate neighbourhood of reacting bovines. If it is true that transmission in nature is effected by an insect vector, it would appear that this particular insect is not present at the Kabete laboratories, or that the presence of some intermediate host other than sheep is necessary for the spread of the disease.

Of interest is the gradual alteration in character of clinical symptoms. For, example, the only typical features shown by the majority of reacting animals in the later passages were a progressive corneal opacity and a dejected, sleepy attitude. Catarrhal discharges were almost absent, and the superficial lymph-glands were less obviously enlarged. On the other hand, the macroscopic lesions found on post-mortem examination of such animals were often fully characteristic.

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Histo-pathological examinations will form the subject of a separate report by the author's colleague (W. Plowright), but it may be said here that the reaction of tissues to the virus in the earlier passages appeared to be proliferative rather than degenerative. Sections of buccal epithelial tissues revealed extensive accumulations of mononuclear cells in sub-epithelial situations, and it seems likely that this interfered with the metabolic processes of the overlying epithelial cells. This would be followed by degeneration, bacterial infection and the appearance of the well-known catarrhal symptoms. The absence of catarrhal discharges, therefore, implies that the " D " strain of virus is changing its pathological behaviour, possibly by exercising a more direct, degenerative effect on certain vital tissues, such as the walls of blood vessels. This is exemplified, to some extent, by the rapid and fatal termination of clinical symptoms in some animals of the later passages.

Failure to filter the virus was not unexpected. The only author to claim successful infection with filtered material is Zanzucchi (1934), but, as already mentioned, it seems not unlikely that he was investigating a disease different in certain fundamental respects from African malignant catarrh. There seems every reason to suppose that the virus is firmly attached to cells, probably of the lymphocytic series. Daubney (1945) reported that Hudson was unable to elute virus from lymph-gland cells, and in the present series of experiments rapid freezing and thawing of lymph-gland material was also unsuccessful. On the other hand, it is not impossible that the virus may be of such a size as to preclude passage through the usual type of filters. Further filtration experiments are at present being undertaken, using graded gradocol membranes.

Summary

(1) The passage of a virulent strain of the " head and eye " form of bovine malignant catarrh, by gland to gland inoculations, through 19 generations of cattle, is described.

(2) Out of 41 animals used, all but one contracted malignant catarrh. Neither age nor breed appeared to qualify susceptibility.

(3) By the nineteenth passage no significant reduction of incubation period was evident.

(4) No cases of contact infection occurred, although susceptible cattle were at all times in close proximity to reacting animals.

(5) Attempts to filter the virus failed.

(6) Attention is drawn to certain clinical features and lesions peculiar to this series.

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NITROFURAZONE IN THE TREATMENT OF CÆCAL COCCIDIOSIS IN CHICKENS

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Dodd and Stillman (1944) discussed the bacteriostatic action of 5-nitro-2-furaldehyde semicarbazone (nitrofurazone) and other related compounds and the necessity of having a 5-nitro group for maximal bacteriostatic effect. Stillman and Scott (1945) considered the chemical aspects of the compound. Dodd (1946) described the activity of the compound against experimental infections of streptococcus and *Trypanosoma equiperdum* and the pharmacology of the compound was studied by Krantz and Evans (1945). Nitrofurazone was selected for trial against avian coccidiosis by Harwood and Stunz (1949) on the grounds of its high *in vivo* activity against several species of bacteria and the protozoan species *Trypanosoma equiperdum.* These authors found that small quantities of drug controlled losses from experimentally-induced cæcal coccidiosis in fowls. One part nitrofurazone to 9,000 parts of an all-mash diet was effective and only 2.5 per cent of treated chickens died of coccidiosis as against 76 per cent of the untreated controls. They claimed that, quantitatively, nitrofurazone was more effective than other compounds previously used against *Eimeria tenella* infections in chickens. Nitrofurazone was found to be fully effective if first offered to infected chickens at intervals up to 56 hours after initial infection and there was no interference with the development of immunity. No retarding of growth was observed following the feeding of mash containing this compound at therapeutic concentrations. Harwood and Stunz (1949a) pointed out that owing to the efficiency of this drug a range of possibly coccidiostatic compounds differing in structure from those of other known effective coccidiostatic substances had now become available. In a later communication, Harwood and Stunz (1950) showed that nitrofurazone fed continuously at a level of 0.0067 per cent

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of various all-mash feeds proved very effective in preventing outbreaks of coccidiosis. They pointed out that when the diet was abnormally low in riboflavine, 0.0067 per cent nitrofurazone apparently increased the frequency and severity of curled-toe paralysis. Peterson and Hymas (1950) compared, quantitatively, the anticoccidial properties of sulphaquinoxaline, nitrofurazone and nitrophenide against intestinal coccidiosis produced by experimentally infecting chickens with 100,000 oocysts of *E. necatrix*. They found that 0.005 to 0.03 per cent of nitrofurazone mixed in the mash and first given at the time of initial infection markedly reduced losses and that 0.02 per cent gave complete protection, but produced a decline in growth-rate. These observations prompted us to undertake a series of confirmatory experiments to determine the value of nitrofurazone in preventing the development of serious infections and in dealing with established ones.

Technique

1. *Administration of Oocysts.*

(*a*) In all cases where infections were produced by single massive doses, 75,000 sporulated oocysts were administered orally. Reinfections, carried out to determine the chicks' resistance to disease after treatment, were produced by using multiples of the single massive dose administered orally at least 10 days after the last control chick succumbed.

(*b*) Serial infections were carried out by giving the equivalent number of oocysts contained in one dose, i.e., 75,000, over a period of three days. One ml. of the suspension was diluted to 9 ml., and 1 ml. of the diluted suspension was given morning, noon and evening for three days to each chicken. In other experiments half the total number of oocysts was used.

2. *Preparation of Medicated Ration.*

A concentrated premix of nitrofurazone ("Nefco") was used for preparing the ration in the majority of experiments. "Nefco" contains nitrofurazone in an oat-feed base containing added riboflavine together with an inert pigment to facilitate even distribution of the premix throughout the mash. The medicated ration was prepared by adding "Nefco" to a small quantity of mash and gradually incorporating more mash until a homogeneous mixture was obtained. Free nitrofurazone mixed with the food was used in the earlier experiments and no riboflavine supplement was added.

3. *Oocysts in the Fæces.*

In a few experiments determinations were made by the numbers of oocysts present in the fæces. These were made by the McMaster technique for counting helminth ova.

4. *Preparation of Cæcal Material for Histological Examination.*

Tissues for histological examination were taken from treated and untreated infected chickens killed at the required time. The tissues were fixed in Bouin's fixative. Sections were cut at a thickness of 5 microns and stained by the iron hæmatoxylin method of Heidenhain. The state of nuclear division within the second generation schizont is an important guide to the coccidiostatic effect of

drugs and the Heidenhain method has in our hands proved to be the most effective means by which the nuclear behaviour can be demonstrated.

5. *Dimensions for Schizonts.*

The dimensions of second generation schizonts exposed in sections of infected cæcal wall were made by *camera lucida* projections on to a card scaled by means of a stage micrometer. The dimensions given in the text are averages of those of varying numbers of schizonts.

Experimental

The Effect of Nitrofurazone on Mortality from Experimentally-induced Cæcal Coccidiosis.

Preliminary experiments were carried out on lines similar to those followed in testing other drugs. In most instances chickens were fed large numbers of sporulated oocysts of *Eimeria tenella* after or before the initiation of medication which was continued in most cases for seven days in all. Screening tests must not be confined to the single dose technique but should include methods more closely resembling those occurring in the field. To meet this we have included tests conducted in pens containing communities of chickens. In these tests artificially-infected chicks were allowed to contaminate the litter in the pen so that susceptible chickens picked up their coccidial infections in a natural manner. The drug to be tested was not offered to the chickens until the majority of oocysts had been passed on to the litter by the artificially-infected chicks.

Experiment 1. Infections of two-week-old BR X BL cockerels were obtained by serial doses of 4,000 sporulated oocysts of *E. tenella* administered three times a day for three days, thus administering 36,000 oocysts in all. Treatment with a medicated feed containing 0.03 per cent nitrofurazone was started 24 hours before, at time of, and 24 hours after the administration of the first doses of oocysts in each series, and was continued for seven days. An untreated but infected group of chicks was run as controls. By these means the value of the drug in controlling gradually increasing infections was determined. The results are shown in Table 1.

TABLE 1.

The Effect on Mortality of Feeding 0.03 *per cent Nitrofurazone in the Feed.*

Time treatment started in relation to infection with first dose of oocysts (in hours)	*Chickens dying from cæcal coccidiosis*									
	1	2	3	4	5	6	7	8	9	10
24 before	+	—	—	—	—	—	—	—	—	—
0	+	—	—	—	—	—	—	—	—	—
24 after	—	—	—	—	—	—	—	—	—	—
Controls	+	+	+	+	+	+	+	+	+	—

Nitrofurazone at a concentration in the feed of 0.03 per cent gave almost complete protection when given before or at time of first infection. No deaths occurred when treatment was delayed until 24 hours after first infection.

Experiment 2. Three concentrations of nitrofurazone, 0.02, 0.03 and 0.04 per cent in the feed, were used. Infection of groups fed on these concentrations and an untreated control group was obtained by the administration of four massive doses of sporulated oocysts on two consecutive days to each of fifty-eight

chicks of each group. Treatment of the three test groups was started 24 hours after initial infection with oocysts and was continued for seven days. Nine of the 0.02 per cent treated, eight of the 0.03 per cent treated and fourteen of the 0.04 per cent treated chickens died of acute cæcal coccidiosis in contrast to forty-seven from the control group. A concentration of 0.04 per cent proved slightly toxic or unpalatable to the chickens and their reluctance to feed accounts for the larger number of deaths in this group.

Experiment 3. This experiment was carried out to determine the effect of feeding a 0.03 per cent medicated ration for seven days on infections produced by single dosing of sporulated oocysts of *E. tenella*. Treatment was started at different times in relation to the administration of the single dose of oocysts, i.e., 24 hours before, at the time of, and at 24 and 48 hours after the chicks received their doses of oocysts. Ten chickens were used in each group. The results of these trials are set out in Table 2.

TABLE 2.

Showing the Effect of 0.03 *per cent Nitrofurazone on Infections Produced by Single Doses of Oocysts of E. tenella.*

Method of infecting chickens	*Time (in hours) of start of treatment in relation to the initial infection*	*Deaths from cæcal coccidiosis* 1	2	3	4	5	6	7	8	9	10
Single ...	24 before ...	+	—	—	—	—	—	—	—	—	—
	0 ...	+	—	—	—	—	—	—	—	—	—
	24 after ...	—	—	—	—	—	—	—	—	—	—
	48 after ...	—	—	—	—	—	—	—	—	—	—
	Controls ...	+	+	+	+	+	+	+	—	—	—

A marked protection was provided by treatment in all cases.

Experiment 4. (*a*) Each chick of two groups of fifty-five chicks per group was given a single dose of oocysts. Forty-eight hours later one group (Group 1) was offered a 0.03 per cent medicated ration for seven days. The chicks in the other group (Group 2) remained untreated and served as controls. A third group (Group 3) of forty-six chicks was retained uninfected and untreated until the second part of the experiment. Three chicks from the treated group and forty-seven control chicks from Group 2 died of acute cæcal coccidiosis. There was some evidence of toxic effects in several of the treated chicks and although six died between the 72nd and 168th hour after the start of treatment they were entirely negative for coccidiosis. (*b*) Twelve survivors from the treated group (Group 1) and twelve chicks from the hitherto uninfected and untreated group (Group 3) were fed 150,000 sporulated oocysts on the tenth day after the deaths in the control group (Group 2). None of the chicks from Group 1 succumbed, but eleven of the twelve control chicks from Group 3 died of acute cæcal coccidiosis.

A firm immunity to disease had evidently been developed in the treated chickens of Group 1 as a consequence of the first infection.

Experiment 5. The concentration of nitrofurazone was reduced to 0.022 or 0.011 per cent in this experiment. Three groups of ten chicks each were

infected with 75,000 sporulated oocysts and were then treated as follows: Group 1 was given access to a 0.011 per cent medicated ration 24 hours later; Group 2 was given access to a 0.011 per cent medicated ration 48 hours later; and Group 3 was given access to a 0.022 per cent medicated ration 48 hours later. Treatment was continued for seven days. A fourth group was similarly infected but received no nitrofurazone. The results of this experiment are given in Table 3.

TABLE 3.

Showing the Effect of Feeding Different Concentrations of Nitrofurazone in Food after Initial Infection.

Group	*Concentration of nitrofurazone in food*	*Delay of treatment in hours*	*No. of chicks in group*	*Deaths from cæcal coccidiosis* 1	2	3	4	5	6	7	8	9	10
1	0.011 per cent	24	10	+	+	—	—	—	—	—	—	—	—
2	0.011 per cent	48	10	+	—	—	—	—	—	—	—	—	—
3	0.022 per cent	48	10	—	—	—	—	—	—	—	—	—	—
4	Nil (controls)	—	10	+	+	+	+	+	+	+	+	—	—

A repeat experiment carried out on similar lines failed to give such good results as four of the ten chickens in Groups 1 and 2 succumbed. It is possible that these differences in results can be accounted for by an unequal distribution of the compound in the food rather than by any individual variations in the chicks themselves. In a further trial eighty one-week-old chicks were each infected with 75,000 oocysts and forty of them received treatment with 0.022 per cent nitrofurazone in the food one day later and for a further five days. The other group remained untreated. Twenty-three of the forty untreated and one of the forty treated chicks died of acute cæcal coccidiosis.

Experiment 6. Four groups of one-week-old chicks were each made up of ten Barred Rock and ten Brown Leghorn cockerels. Group 1 was infected with 75,000 sporulated oocysts and 24 hours later was given access to a ration containing 0.011 per cent nitrofurazone for six days. Group 2 was not infected but received the medicated ration. Group 3 was infected but received unmedicated ration, and Group 4 was reserved as a control group to "challenge" doses which were administered later to the survivors of Groups 1 and 2. Seven of the twenty chickens in Group 1 and fifteen of the twenty chickens in the control group 3 died from acute cæcal coccidiosis.

Ten days after the last death in Group 3 the survivors from Group 1 and the chickens of Groups 2 and 4 were each fed 220,000 sporulated oocysts. None of the thirteen survivors of Group 1, nineteen of the twenty chickens from Group 2 and seventeen of the twenty chickens from Group 4 died from acute cæcal coccidiosis. A firm resistance, therefore, had been established in the survivors of Group 1 following the first infection in spite of treatment.

Experiment 7. In this experiment the coccidiostatic effect of a ration containing 0.011 per cent nitrofurazone was again studied in chicks receiving serial or single infective doses of oocysts. Treatment was delayed for 24 hours in both cases. Two control groups were used to cover the serially-administered

and single-dose groups. Twelve or thirteen chicks were used in the groups. This experiment was also designed to determine whether any significant difference existed between the results obtained by the use of the two methods of infection. The results are set out in Table 4.

TABLE 4.

The Coccidiostatic Effect of 0.011 *per cent Nitrofurazone in the Food on Infections Produced by Single- or Serial-dosing when Treatment was Delayed until* 24 *Hours after the Single or First of the Serial Doses was Administered.*

Method of infecting chickens	*Treated (T) or Untreated (U)*	*Deaths from cæcal coccidiosis* 1	2	3	4	5	6	7	8	9	10	11	12	13
Single ...	T	+	—	—	—	—	—	—	—	—	—	—	—	
	U	+	+	+	+	+	+	+	+	+	+	+	+	
Serial ...	T	—	—	—	—	—	—	—	—	—	—	—	—	—
	U	+	+	+	+	+	+	+	+	+	+	+	—	—

The results suggest that nitrofurazone is of value when employed as a prophylactic or as a means of controlling established infections.

Experiment 8. The object of this experiment was to determine the effect of nitrofurazone on infections picked up before and during treatment. The drug used in this way would be similar in its effects to a continuous treatment which farmers might employ to prevent outbreaks of coccidiosis. Sporulated oocysts were administered to groups of twelve chicks as follows: Groups 1 and 1a both received approximately 12,000 oocysts on each of six alternate days; Groups 2 and 2a both received approximately 18,000 oocysts on each of four alternate days; Groups 3 and 3a both received approximately 24,000 oocysts on each of three alternate days; and Groups 4 and 4a both received approximately 36,000 oocysts on each of two alternate days. Groups 1, 2, 3, and 4 were given access to 0.011 per cent nitrofurazone 48 hours after they had received the first dose of oocysts and treatment was continued for fourteen days. Groups 1a, 2a, 3a, and 4a, which were untreated, served as controls. The results, which are summarised in Table 5, show that the drug gave good protection under these conditions.

TABLE 5.

Showing the Coccidiostatic Effect of a 0.011 *per cent Nitrofurazone Feed on Progressive Infections Initiated Before and Continuing Beyond the Start of Treatment.*

Group	*Deaths from cæcal coccidiosis* 1	2	3	4	5	6	7	8	9	10	11	12
1	+	+	—	—	—	—	—	—	—	—	—	—
1a	+	+	+	+	+	+	+	+	+	—	—	—
2	+	+	+	+	—	—	—	—	—	—	—	—
2a	+	+	+	+	+	+	+	+	+	+	+	+
3	+	—	—	—	—	—	—	—	—	—	—	—
3a	+	+	+	+	+	+	+	+	+	—	—	—
4	+	+	+	+	—	—	—	—	—	—	—	—
4a	+	+	+	+	+	+	+	+	+	+	+	+

Experiment 9. Two pens were each populated with (1) ten two-week-old chicks each of which had been infected with 7,500 sporulated oocysts, (2) fourteen two-week-old uninfected chicks which were allowed to pick up the oocysts passed by (1), and (3) seven days later a group of twenty-two one-week-old uninfected chicks was placed in the pen to pick up oocysts passed by (1) and (2), and finally (4), twenty-nine one-week-old uninfected chickens were introduced into each pen sixteen days later and would be able to pick up oocysts passed by the members of the other groups. One pen was treated for the duration of the experiment with 0.011 per cent "Nefco" nitrofurazone in the food. Treatment was started six days after the commencement of the experiment.

The other pen was left untreated and the chicks served as controls. Sawdust litter was used for the first week and was followed later by chopped oat straw which was kept moist to ensure the viability of the oocysts. The outcome of this trial is shown in Table. 6.

TABLE 6.

Deaths from Cæcal Coccidiosis in Infected and Treated, and Infected and Untreated Pens of Chickens.

Group	*Number of chicks in each pen*	*Deaths from cæcal coccidiosis*	
		Treated pen	*Untreated pen (controls)*
1	10	0	0
2	14	0	0
3	22	0	10
4	29	0	29

In this experiment nitrofurazone proved highly effective in preventing deaths from cæcal coccidiosis among chicks exposed to an accumulated ground infection.

Experiments 10-15. A series of small-scale experiments was undertaken to determine the coccidiostatic effect of feeding 0.011 per cent nitrofurazone in the food to chicks which had received their initial infections 24 and 48 hours previously. The results, which are shown in Table 9, show the effect of administering nitrofurazone to chickens with established heavy infections of *E. tenella*. Infections were produced by feeding each chick with 75,000 sporulated oocysts. Treatment was continued for seven days in all cases.

TABLE 9.

Showing the Effect of Feeding to Heavily-Infected Chicks 0.011 *per cent Nitrofurazone in the Ration when Treatment was Commenced at Different Times after Receiving their Initial Infections.*

Experiment No.	*Time after initial infection that treatment was started (in hours)*	*No. of chicks in each group*	*Deaths from cæcal coccidiosis*	
			Treated groups	*Untreated groups*
10	24	10	2	10
11	24	10	3	10
12	24	12	1	10
13	24	20	7	15
14	24	10	2	8
15	48	20	5	15

The above results show that nitrofurazone at 0.011 per cent in the food gives considerable protection when applied to established infections of *E. tenella* within the time limits tested.

Experiment 16.—The effect of a 0.011 per cent nitrofurazone mash diet on the development of *E. tenella* was studied by taking sections of the walls of cæca of chickens which had been artificially infected and treated either immediately or from the 24th or 48th hour after infection. These sections, and sections of the cæca from untreated infected chicks, were searched for stages and compared. Table 10 summarises the observations made.

TABLE 10.

The effect of 0.011 *per cent nitrofurazone on the development of E. tenella.*

Start of treatment after initial infection (in hours)	*Times after initial infection that cæcal sections were taken*		
	96 *hours*	120 *hours*	144 *hours*
	Stages observed		
0	—	—	Some 2nd g. schizonts (discharged) 30 x 20 microns. Micro- and macrogametocytes
24	—	Few 1st g. schizonts (some abortive) 20 x 20 microns	A few gametocytes
48	Some 1st g. schizonts (some abortive) 20 x 20 microns	2nd g. schizont with merozoite formation, 30 x 23 microns	2nd g. schizont 30 x 20 microns. Micro- and macrogametocytes
Controls	Early 2nd g. schizonts 15 x 10 microns	2nd g. schizonts complete merozoite formation, 32.1 x 22 microns	2nd g. schizonts. 50 x 36 microns and advanced micro- and macrogametocytes

Nitrofurazone produces a marked retardation in the rate of development of *E. tenella* in the chicken as well as a reduction in the dimensions of the second generation schizont and in this way resembles in action that of most known coccidiostatic compounds.

Experiment 17.—Nitrofurazone at 0.011, 0.022 and 0.033 per cent in the food was offered to groups of chicks immediately after the chicks had received 7,500 sporulated oocysts of *E. tenella*. An untreated infected group was run for comparison. Fæcal examinations were made on the seventh to eleventh days inclusive. An uninfected group was also kept to serve as a control against the possible entry of extraneous infections. The numbers of oocysts per gramme of fæces passed by each group are given in Table 11.

TABLE 11.

The number of oocysts per gramme of fæces passed by different groups of chicks over a five-day period.

Group	*Percentage concentration of nitrofurazone in the feed*	*Days after first doses of oocysts were administered*				
		7	8	9	10	11
		Number of oocysts per gramme of mixed fæces				
1	0.011	36,000	9,700	41,700	10,800	7,300
2	0.022	5,300	3,400	27,400	3,800	2,900
3	0.033	100	400	2,900	1,000	2,500
4	Infected controls	324,000	262,000	141,000	66,000	3,100
5	Uninfected controls	—	—	—	—	—

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The numbers of oocysts passed by the infected and untreated control group greatly exceeded those passed by the nitrofurazone treated chickens and the greatest number was passed on the seventh day. Of the treated groups, the one receiving the least nitrofurazone (group 1) passed the largest number of oocysts on the seventh day. In all the treated groups the peak of oocyst-production occurred on the ninth day, which indicated a retardation in the rate of the development of the parasites. At 0.033 per cent the suppression of oocyst-production was considerable. Nitrofurazone probably destroys some of the individual stages and inhibits the development of the rest. At the same time, the apparent destruction of stages may, in fact, be due to a prolonged period of inhibition in which case fæcal examinations should be made over a considerably longer period than five days although a study of cæcal sections suggests destruction.

The Effect of Nitrofurazone on the Weight Gain of Chickens

Experiment 18.—Two groups of uninfected chicks were used. Both groups consisted of 14 females and 5 males, Barred Rock x Brown Leghorn day-old chicks. One group received a medicated ration containing 0.011 per cent nitrofurazone from a week old and for 28 days, after which the chickens were returned to normal feed for ten days followed by a further period of medication for 21 days when they were once again returned to a normal ration. The other group received a normal ration throughout. Both groups were weighed at intervals during the experiment. The results are given in Table 12.

TABLE 12.

Showing weight gains (in ounces) of nitrofurazone-treated and untreated uninfected chickens at various intervals during the treatment of the one group.

No. of days after start of treatment	*Average weight gains (in ounces) of chickens*			
	Nitrofurazone group		*Normal group*	
	Males	Females	Males	Females
7	2.39	2.39	2.43	2.36
21	6.54	6.06	7.08	6.43
28	9.39	8.82	9.72	9.04
All chickens on normal rations for ten days followed by 21 days of treatment				
59	30.64	27.34	30.88	26.58
Treatment ceased				
73 (14 days after cessation of treatment)	43.64	37.14	43.68	34.28

At the end of 28 days' treatment the weight gains of the treated chickens were lower than those of the normal group. A ten-day rest from treatment followed by a further 21 days on medicated food restored the weight gains of the treated chicks to much the same level as that of the controls. The final weights of the treated group taken 14 days after final cessation of treatment compared very favourably with those of the chicks on normal feed.

Discussion

Nitrofurazone is an extremely effective coccidiostatic compound when mixed in food at low concentrations. Good protection was afforded to chickens

which had received heavy experimental infections with *E. tenella* 48 hours before the commencement of treatment with 0.022 per cent of the drug in the food. Treatment should be continued for seven days. This concentration of the drug is to be recommended for the treatment of established infections of cæcal coccidiosis. Where there is a history of cæcal coccidiosis on farms a preventive treatment may safely be adopted when chicks are put into new quarters; this takes the form of feeding a 0.011 per cent medicated ration over a period of ten days. The comparative weight gains of treated and untreated chicks show that the length of treatment with a 0.011 per cent medicated feed may be exended to one month without seriously retarding weight gain. There is no evidence that treatment of chicks exposed to infections of *E. tenella* interferes in any way with the development of their resistance to this species. Where chicks are maintained under conditions favouring a substantial increase in the litter-population of oocysts and the intake of sporulated oocysts, as might occur by adding susceptible chicks to already infected pens, low concentrations of nitrofurazone may fail to prevent outbreaks of disease. Under these circumstances a seven-day treatment at the higher concentration of 0.022 per cent nitrofurazone should effectively control the outbreaks.

As the observations of Harwood and Stunz (1950) showed that nitrofurazone increases the frequency and severity of curled-toe paralysis in chicks when the diet is deficient in riboflavine, it is recommended that the drug be incorporated in a premix containing additional riboflavine. In view of Becker's findings (1942) that an excess of riboflavine in the diet of rats reduced the multiplication of *Eimeria nieschulzi* in the host, our preliminary experiments were carried out without the addition of riboflavine to the diet, to determine the effect of nitrofurazone in the absence of excess riboflavine. There was no significant difference in mortalities between the groups on medicated ration and those on medicated ration with the riboflavine supplement.

The action of nitrofurazone on the coccidia resembles that of the coccidiostatic sulphonamides. There is a delay in reaching the peak of oocyst-production and smaller numbers of oocysts are formed in comparison with the untreated control groups. A study of sections of cæca from treated and untreated infected chicks also suggests that a number of the intracellular asexual stages of the life-cycle are destroyed while the development of others is inhibited.

Summary and Conclusions

(1) Nitrofurazone is an effective coccidiostatic agent and is a valuable means of controlling established infections of cæcal coccidiosis when fed to chickens at a food concentration of 0.022 per cent for seven days.

(2) Nitrofurazone is of value as a preventive when fed at a concentration in the food of 0.011 per cent for ten days to chicks kept on litter which may be heavily infested with coccidia.

(3) Nitrofurazone permits the normal development of immunity to cæcal coccidiosis in chicks exposed to infections of *Eimeria tenella* during treatment.

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(4) The action of nitrofurazone is partly schizontistatic and partly schizonticidal.

Acknowledgments

We are indebted to Messrs. A. J. White, Ltd., for supplies of "Nefco" nitrofurazone and to Miss E. A. Robb for technical assistance.

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A CARDIAC ABNORMALITY

Hypoplasia of the right ventricle. Atresia of the pulmonary artery

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CARDIAC MALFORMATIONS are common congenital defects, and many different forms from man and animals have been described. The combination of pulmonary atresia and right ventricular and tricuspid hypoplasia, described in this paper, is one of the rarer varieties and, although recorded on a number of occasions in the human subject, it is believed that this is the first record of such an abnormality in the dog.

Miss Audrey Johnson, of the Royal Veterinary College, was responsible for the clinical record.

Subject.—A three months cocker spaniel dog.

History.—Nothing is known of the early history, as the dog was purchased by its final owner only four days previous to the first clinical examination. At the time of sale it appeared to the purchaser to be lively and normal in every respect. During the next few days it became apathetic, lost interest in food, and vomited on several occasions. The owner brought it for examination because of respiratory distress.

Clinical examination.—The puppy was well developed and in good general condition. Temperature normal; heart rate accelerated, but heart sounds normal; moderate hyperpnœa; visible mucous membranes pale. Radiographs of the chest showed no abnormality apart from a considerable enlargement of the heart with a flattening of the anterior contour apparent in the lateral view.

Diagnosis. — Congenital cardiac disease — the symptoms not permitting specification of the exact anomaly.

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Course.—The condition of the animal deteriorated during the next few days, with intensification of the symptoms—increased frequency of vomiting, marked increase in the respiratory rate with entirely abdominal respirations, increasing tachycardia with development of irregularity. Six days after the first examination, the puppy was presented in a state of collapse, with a temperature of 99° F., and was destroyed.

General post-mortem findings.—General condition good; marked ascites; passive venous congestion, especially of the liver; lungs congested and very œdematous; lungs and systemic circulation supplied by a common trunk. The heart was preserved for examination.

Description of the Heart

The heart, which measured 9.5 cm. in its long axis, was greatly enlarged mainly due to a dilated left ventricle. The longitudinal sulci demarcated a diminutive right ventricle confined to the anterior and dorsal part of the ventricular mass.

Left atrium.—Some dilatation and hypertrophy. A membranous flap, arising from the septum, projected anteriorly into this chamber and partially covered a circular defect in the interatrial septum, approximately 1.5 cm. in diameter. Otherwise this chamber was normal.

Left ventricle.—Appeared much enlarged, and as the walls were of only half the normal thickness, a greatly increased chamber capacity resulted. No other abnormality.

Right atrium.—Considerable dilatation and hypertrophy. The atrioventricular opening was hypoplastic and, except for a narrow slit, completely closed by a continuous thickened valve. A powerfully developed crista interveniens extended on to the atrial floor behind the ostium; immediately posterior to this, the coronary sinus opened dorsally. The presence of an interatrial septal defect has already been noted.

Right ventricle.—Very markedly hypoplastic. The walls were thick and the actual capacity was only 1 to 2 c.c. The roof was almost entirely formed by the atrioventricular valve, while the conus arteriosus part was represented by a diminutive anterior cleft. There was no trace of the pulmonary valve, or artery. The interventricular septum was complete. A blood clot entirely occupied this chamber, which formed a blind non-functional appendage of the right atrium.

In none of the chambers was there any trace of recent organic disease of the heart.

Blood Vessels

The *single artery* arising from the heart had been cut about 1½ cm. above the semilunar valve, making it impossible to determine the arrangement of the blood supply to the lungs. The pathologist reported that the aorta and pulmonary artery arose by a short common trunk—a description that, at first sight, suggests the identification of the solitary vessel as a truncus arteriosus

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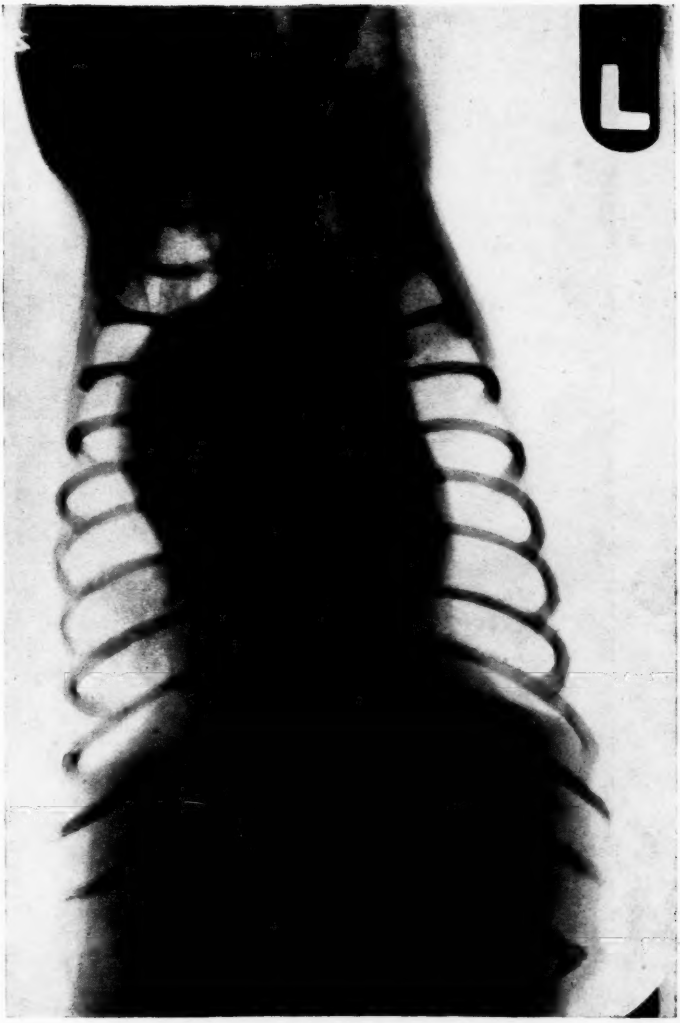

FIG. 1
Ventro-dorsal radiograph showing over-all enlargement of heart.

(Article by Dyce, page 57)

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FIG. 2

Antero-right lateral view of heart showing diminutive right ventricle and hypertrophy of left ventricle.

(*Article by Dyce, page* 57)

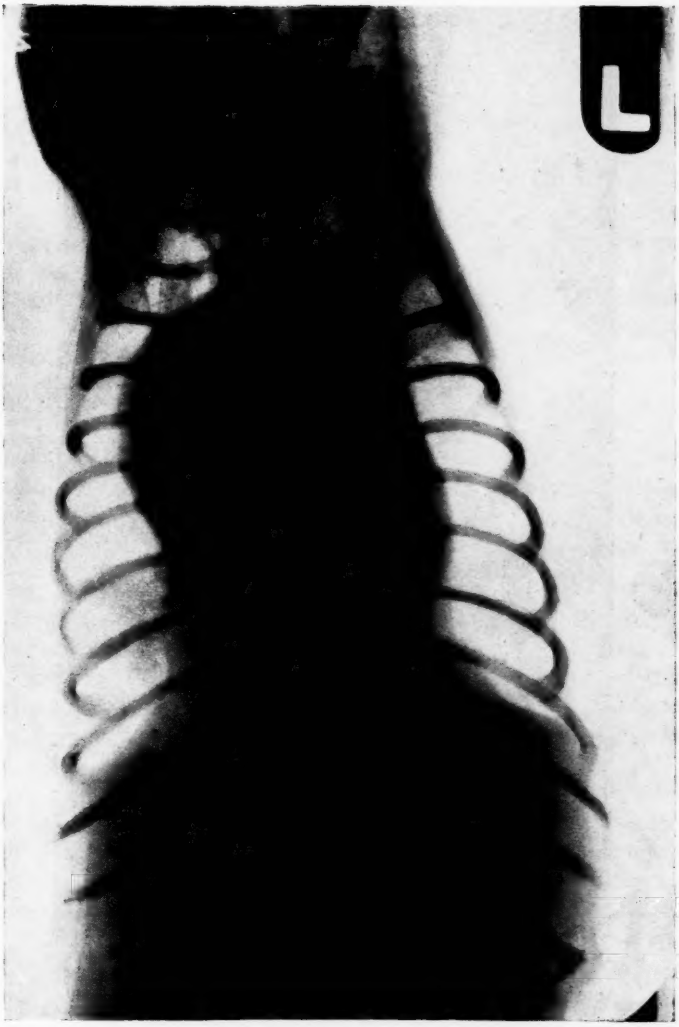

FIG. 1
Ventro-dorsal radiograph showing over-all enlargement of heart.

(*Article by Dyce, page 57*)

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FIG. 2
Antero-right lateral view of heart showing diminutive right ventricle and hypertrophy of left ventricle.

(*Article by Dyce, page 57*)

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communis persistens. Humphreys (1932), reviewing the question of this identification, has established a number of criteria that must be satisfied before this diagnosis is acceptable; applying these criteria in this case, it was found that in the essential features of origin from the left ventricle, number and distribution of semilunar cusps and disposition of coronary arteries, the solitary trunk differed from a true truncus arteriosus communis. It is therefore to be assumed that the common trunk had divided and that the pulmonary artery had become atretic at a later stage, leaving the aorta alone. It is possible that the distal part of the pulmonary artery remained patent and that the pathway to the lungs was via aorta, ductus arteriosus, and the distal segment of the pulmonary artery. Other arrangements such as increase of the bronchial arteries or the development of a wholly anomalous pulmonary blood supply are, however, possible. In the absence of the lungs and associated vessels, further speculation is bound to be without profit.

The *veins* were normal.

Anatomical diagnosis.—Dilated right atrium; hypoplastic right ventricle and tricuspid valve; interatrial septal defect; proximal pulmonary atresia with persistent ductus arteriosus(?).

Ætiology and Pathogenesis

It is rarely possible to be precise concerning the ætiology of a congenital defect, even to the extent of incriminating a genetic or an environmental origin. This case is no exception and, while admitting the possibility of a pre-natal infection, nothing can be established concerning the cause of the malformation. One can suggest, however, that the disturbance occurred at the stage of development following the fusion of the ventricular and spiral septa, when the bulbus cordis is being incorporated in the right ventricle. This period is believed to be an especially critical one in the development of the human heart and many investigators, following the work of Keith, have shown that many of the abnormalities of the human heart are to be traced to maldevelopment at this stage. Cohrs (1949), however, states that these defects are relatively much less common in animals than in man.

It is not necessary to postulate independent origins for the several anomalies, as once the pulmonary circuit is closed at any point the resulting inactivity of the right ventricle is sufficient to account for the hypoplasia of this chamber, and of the tricuspid valve. The presence of a passage through the atrial septum is an obvious requirement for the continuation of the circulation, but this, in the shape of the foramen ovale, represents the normal condition in the fœtus and there is no reason why fœtal development should not proceed normally. After birth, however, the mixing in the heart of the pulmonary systemic venous returns, results in the distribution of imperfectly oxygenated blood to all tissues and organs, which suffer according to their several susceptibilities. The heart muscle must have been affected with the other tissues and have been made less able to cope with the other demands made upon it.

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The additional effect on the heart due to the altered course of the circulation can be analysed approximately. The right atrium received the normal return of blood from the body; this blood, denied its normal exit into the right ventricle, could only escape into the left atrium through a constricted opening and against the resistance due to the pulmonary return, reduced though this may have been. As a result the pressure in the right atrium rose and, transmitted through the great veins, led to a passive venous congestion: the atrium itself responded by hypertrophy and dilatation. The left atrium received a double flow of blood and conditions similar to those in the right atrium were created; in this case the result was a pulmonary congestion and œdema, and again dilatation and hypertrophy—less marked, however, possibly due to the greater ease of escape for the blood.

The left ventricle, called upon to receive the increased flow and to drive this to both body and lungs, responded by dilatation.

The most interesting feature of this case was the ability of the animal to survive for so long and with so little apparent inconvenience, indicating that, whatever the precise arrangement, the lungs received a fair supply of blood. It is surprising that cyanosis was never observed, as this is an invariable symptom in human infants afflicted with this anomaly (Brown, 1950; Taussig, 1936, 1947). It has often been observed that the organism can tolerate congenital conditions that if acquired later would make death inevitable and immediate; and presumably during fœtal and early post-natal life, when activity is least, the organism can adapt itself to the condition. The eventual precipitate deterioration may be accounted for in two ways: a delayed closure of the ductus arteriosus, or the inability of the heart to make further compensation and the onset of decompensation and heart failure.

Acknowledgments

My thanks are due to Miss Audrey Johnson, of the Royal Veterinary College, for permission to make use of her clinical record of this case. Acknowledgment is also due to Miss Harrod, who was responsible for the radiograph, and Mr. Burgess, for the photographs of the heart.

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NOTES ON HUMAN THORACIC SURGERY
Observations Following a Week's Attendance at a Surgical Unit for Thoracic Surgery

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Surgical Intervention Within the Thoracic Cavity.

In human surgery, surgical intervention within the thoracic cavity (with the exception of operations on the heart itself) has now passed the experimental stage, and while the smaller details of the technical procedure are, perhaps, liable to slight modification, the manipulation which may be undertaken successfully are thoroughly understood, and extensive operations are undertaken daily by those who are specialists in this field. The work, however, is of great delicacy, and demands very considerable surgical skill and a thorough understanding of the physiology of the delicate viscera involved. It is necessary also to have devoted considerable thought to the post-operative sequelæ which are closely connected with fluid collections, air leaks and mediastinal displacements. It is not the purpose of this paper to discuss the possibility of a general application of this branch of surgery to veterinary practice, but to describe the technique employed in man, in the hope that this may be of use and interest to the veterinary practitioner. The remarks and observations appended below are the result of my being permitted to watch my friend, Mr. B. J. Bickford, operating at Liverpool, and I wish to express by warmest gratitude on him both for allowing me to be present and for the great pains he took to ensure that each step of the technique was made clear to me. I wish to express also my sincere thanks to Miss E. C. N. Fenton, the anæsthetist, for her kindness in explaining to me with great care the difficult and delicate question of the anæsthesia—of the supremest importance for the successful outcome of the operation. I was deeply impressed throughout the operations by the great confidence displayed, the intrinsic honesty of the technique, and the complete absence of any scientific "side."

Indications

Pulmonary tuberculosis, bronchiectasis, primary (bronchial) carcinoma and other neoplasms of the lungs, empyema, œsophageal carcinoma, and foreign bodies in the bronchi and œsophagus are the most common conditions which call for intrathoracic surgery, and in most of these cases it is necessary to enter the pleural cavity itself. It should be noted, however, that in conditions affecting the ribs, or where thoracoplasty (the obliteration of a part of one of the pleural cavities) is called for, the manipulations may in many cases be performed extra-pleurally.

Diagnosis

Certain and accurate diagnosis is an essential preliminary to operation, and this may be brought about by the use of X-rays or the bronchoscope, or both

combined. The bronchoscope is essentially a tube with a small distal electric bulb to provide light; the lumen is as wide as is consistent with passing down the air tubes. With this instrument all the lobes of the lung can be inspected, together with the openings of their main segmental branches; inflammatory changes can be recognised, the exudation of blood or pus and neoplasms, strictures or foreign bodies can be discerned. Usually, the latter can be removed by suitable forceps, and small portions of abnormal tissue can be removed by biopsy forceps for examination. In cases where the bronchial tree is thought to be involved, bronchography is most useful in giving an idea of the anatomy of this structure, since it will show the relation of the bronchi to other shadows, and may indicate if such a shadow is in the lung or outside it; it will also indication obstruction or dilatation. A bronchograph may be obtained by introducing lipiodol in a cold viscid state into the trachea by injection through the cricothyroid membrane; good results may also be obtained by anæsthetising the patient deeply (with, say, ether), and while in this state pulling forward the tongue and pouring a quantity (20 c.c. in a five-year-old child) of cold viscid lipiodol into the mouth of the trachea—the deep inspirations obtaining at this stage of anæsthesia will suck the substance down into the tubes, while at the same time its viscosity will prohibit its passing into the smaller passages and so bringing about suffocation. Should alarming symptoms supervene with this technique the patient should be held upside-down, when the lipiodol will run out of the mouth.

Anæsthesia

Because of the great respiratory embarrassment that occurs with uncontrolled respiration with the thorax opened, and the great movement that occurs with each respiration, it was formerly impossible to perform any delicate manipulations within the thoracic cavity. The first solution (apart from the not very satisfactory one of performing operations under local anæsthesia with deep basal narcosis) was to use so much anæsthetic agent that the respiratory movement was almost brought to a stop by depressing the medullary centre. This could be done with cyclopropane and a high concentration of oxygen, but was not particularly safe, and in addition there is great risk of explosion if the diathermy knife is to be used. Within the last few years the device of using carefully controlled doses of tubo-curarine to produce muscular paralysis and thus to abolish respiratory movements has been tried, and has been found to be very useful. There is no doubt that it gives the most quiet operative field possible, and the patients stand even very prolonged operations very well.

In nervous children a preliminary narcosis is brought about by administering a dose of pentothal per rectum, but normally the first step in producing anæsthesia is by giving a test dose of 5 mgm. of tubo-curarine into a convenient vein, and if no abnormal symptoms supervene a full dose of round about 15-20 mgm. of the drug is then administered (normal adult). Before the oppressive effects of the curare are felt by the patient, 0.4 gm. of pentothal is given intravenously. Immediately a short rubber tube is passed down the trachea

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and the space between the tube and the trachea is obliterated by inflating a thin rubber cuff. A 50 per cent mixture of nitrous oxide and oxygen is then administered, the anæsthetist inflating the lungs rhythmically by manual pressure on a rubber bag containing a mixture of these two gases. It will be appreciated that the oxygenation of the patient's blood now depends entirely on the care of the anæsthetist, for with the respiratory muscles paralysed by the curare the patient is incapable of breathing for himself. Anæsthesia is kept very light throughout the operation, the patient making movements with his hands and opening his eyes on occasion. This light anæsthesia reduces the risk of shock, which is increased if the patient is allowed to become cyanotic. Should the anæsthesia become so light as to be in danger of passing off, an additional small dose (0.1 gm.) of pentothal may be given intravenously. At the same time the pentothal is not exclusively responsible for the state of anæsthesia, its action being reinforced by the action of the nitrous oxide. A small point of practical importance: the intravenous needle may be left in the vein and prevented from being blocked by thrombus by feeding it by gravity with a solution of normal saline. The anæsthetist takes as his guides the state of the patient, his colour, the pulse, and the "feel of the bag." Since a closed circuit is used the carbon dioxide exhaled must not be allowed to accumulate, and this is absorbed by a cylinder containing soda-lime: such a cylinder will last about six hours. A narrow suction catheter may be passed down the endotracheal tube in order to remove secretions or exudate accumulating in the air passages during operation.

At the termination of the operation the quantity of oxygen is increased, and this, together with the weakening effects of the curare, produces slight respiratory movements on the part of the patient: 1/50 gr. of atropine is then given intravenously and then the effects of the curare are combated by administering 5 mgm. of prostigmine — if the atropine is omitted, bradycardia and other undesirable symptoms may supervene. The endotracheal tube is then withdrawn and the patient recovers consciousness a few minutes after the termination of the operation.

Technique

In order to gain access to the thoracic viscera several methods may be used. In all an incision is made in the line of an intercostal space, and in order to gain enough room to separate the ribs widely by some form of self-retaining retractor it is necessary to divide one or more ribs or to resect a good length of one rib. The latter procedure is probably better, since it is easier to close the incision more securely if a rib has already been removed.

For most operations a postero-lateral incision is employed. Occasionally, e.g., for operations on the heart or mediastinum, an antero-lateral approach is employed, but exposure is considerably limited compared to the posterior (owing to the difficulty experienced in separating costal cartilages as compared with ribs), and even for cardiac operations the postero-lateral incision is employed.

The incision is a long one, passing downwards and forwards below the scapula. The latter bone is separated to a greater or lesser extent from its

attachments to the spine by dividing the trapezius and rhomboid muscles in part. The lower part of the incision usually reaches the mid or lower axillary line. It is thus about 12 inches in length, but it is much more important to have sufficient access to the area of operation than to try to save time by making an awkwardly short incision. The length of the incision does not affect its healing, nor is a long incision any weaker than a short one.

After the usual preparation of the site the latissimus dorsi and other muscles are divided and the scapula displaced forward. It is calculated that by using the diathermy knife some 20 minutes are saved which would otherwise have been employed in ligating superficial bleeding points in this primary incision. The ribs exposed, the one to be resected is identified by counting from above downwards. For an upper lobectomy or a pneumonectomy the 5th or 6th rib is resected; for a lower lobectomy, the 7th; for cardiac operations the 4th is chosen.

The rib selected is resected subperiosteally after a longitudinal incision has been made through the periosteum and after the periosteum has been separated from both surfaces of the rib. With the rib removed the pleural cavity is opened, and the anæsthetist relaxes the pressure on the bag and allows the lung to collapse a little—if there are any pleural adhesions they are divided sufficiently to allow of the wound being opened widely (6-8 inches) by spreading with a retractor.

From this point onwards the manipulations employed depend on what is to be done. In operations for resection (of a complete lung or of a lobe) the key to the situation lies in the hilum. By careful dissection, which must be very delicate because of the exceptionally friable nature of the vessels in this region, it is possible to expose the vessels carrying blood to or from the lung. The main pulmonary artery and the superior and inferior pulmonary veins are exceptionally large and must be handled with the utmost care. If they should be accidentally torn the hæmorrhage may be torrential; it is always difficult to control in such circumstances and may prejudice the whole success of the operation. Because of the individual variations in anatomy the rule is to divide whatever hilar structure is exposed most easily, be it artery, vein or bronchus. The blood vessels are divided between ligatures, a common material used being linen thread, which is easily sterilised, is strong, and has no tendency to slip during the tying of the second half of the knot. In the case of the larger vessels a double ligature is placed on the cardiac side of the point of division, and in the case of the main pulmonary vessels it is usual to make one of the ligatures a transfixion one, applied with a fine, curved, round-bodied needle. The bronchus is dissected as clean as possible—this may not be easy, owing to the presence of inflammatory fibrosis in the neighbourhood—and is then clamped on the lung side of the proposed point of division. It is then divided carefully and sutured with fine, interrupted, terminal sutures, usually of an unabsorbable material, such as stainless steel wire or nylon. It is usually not desirable to clamp the bronchus on the proximal side of the point of division, as this may interfere with its vitality to some extent, and the bronchus does not tend to heal particularly well in any event. Having the bronchus open even for the short time between

resection and the completion of the suturing means interference with the administration of the anæsthetic. Until the line of sutures is complete and air-tight it is impossible to inflate the lungs, and all pressure from the anæsthetist must stop, as there is also grave danger of blowing out into the site of operation any exudate which may have accumulated in the lumen of the bronchus. It is usually possible to complete the opening and suturing in stages, when temporary air-tightness can be produced by pressure with a swab. In certain cases a light clamp can be placed on the bronchus to ensure air-tightness.

Often segments of lobes can be removed by dissecting in the hilum until the individual arteries and bronchi are isolated and divided. When they have been secured it is possible to remove the segment concerned by simply stripping it off by strong but careful traction.

Small peripheral segments of the lungs may be removed by a simple wedge-resection—the raw edges being clamped and sutured in the manner commonly applied to other parts of the body. Removal of these peripheral segments is not recommended, however, as the tissue in this area is not so resistant to infection.

In the operation of thoracoplasty, which is used to reduce the size of the chest cavity in order to collapse tuberculous lungs, or in order to obliterate a chronic empyema cavity, the whole of the first two ribs and graduated portions of the succeeding six (for the maximum extent of the operation) are removed. The pleural cavity is not entered, but the apex of the lung and the two layers of the pleura are separated from the mediastinum and chest wall in order to allow them to relax towards the hilum as far as possible.

During a thorocotomy the œsophagus may be opened for the removal of a foreign body, or a portion of the stomach or œsophagus and stomach may be resected if a neoplasm is suspected. The suturing of such an incision or anastomosis must be done with the greatest care to prevent any possibility of a subsequent leak. Interrupted silk sutures are used. The bronchus may be opened for a foreign body—this usually presents no difficulties and the incision is closed carefully with fine sutures of nylon or steel wire so that air-tightness is restored

To close the chest wall, the ribs on either side of the incision may be drawn together and tied with strong linen thread. This provides a firm basis for the muscle sutures above it, since it relieves tension and prevents the tendency to tear apart. The pleura may be sutured with single-strand steel wire and the muscle layers with three-stranded wire or other material, at the surgeon's discretion. The skin may be sutured continuously with nylon. These non-absorbable sutures cause no undesirable reaction on the part of the tissues.

Before closing the chest it is of the supremest importance to insert a drainage tube, the end of which should be at the highest part of the chest cavity. The purpose of this tube is to drain off any exudates which will form, and also to provide an escape for the air which is bound to escape to a greater or lesser degree from the surface of the cut lung for some hours after the operation. If no escape is provided a pneumo-thorax will develop which may lead to the col-

lapse of the lung and displacement of the mediastinum. This tube is left *in situ* for round about 48 hours, and the external end should be led out to rest under about 1 cm. of water in order to establish a water seal.

General Remarks

Both sides of the thoracic cavity may be opened simultaneously.

A time of 2-2½ hours may be regarded as normal for an operation, but in robust patients 5-6 hours may be taken without particular ill-effects.

The pleura is no more vulnerable to infection than the peritoneum, but there is, of course, no omentum to help in overcoming infection.

Shock is connected closely with loss of blood. Blood lost should be made good during the operation by giving a blood transfusion at the same time. The amount of blood lost may be estimated by weighing the swabs, and rather more than twice this amount should be given by transfusion. About 20 oz. is an average blood loss for an adult in thoracoplasty.

OBITUARY

Henry William (Harry) Steele-Bodger

THERE comes a time in the lives of some men when stock is taken of their accomplishments. Alas! for many this means when their death is intimated. Such is the case with Harry Steele-Bodger, who died on January 11, 1952, after a long illness.

Many of our readers knew Steele-Bodger well: there are few in the profession who had not met him—certainly few who did not know of him. The writer is privileged to have been at one time one of the small group whom S.-B. gathered round himself to study how best the veterinary profession could serve the country in the dark days of World War II. Well do I remember the conception of the idea that we, the veterinary profession, should in some way offer our services to the country, in the full knowledge that we had something to give which would be of value. Research work was in progress on bovine mastitis and results were justifying the beneficial use of sulphanilamide in its control. An idea that here was something that could be applied with expectations of increasing milk yield was suggested to S.-B., then President of the N.V.M.A. He at once grasped the idea behind the suggestion that a scheme might be evolved whereby the results of research work could, through the medium of the veterinary profession, be used to benefit the farmer, the nation and the world.

This idea led to the formation of the Survey Committee of the N.V.M.A., which, in turn, was instrumental in bringing into operation the so-called Survey or Panel Scheme (Scheme for the Control of Diseases of Dairy Cattle), a scheme which proved valuable, not only in controlling some of the major diseases of dairy cattle, but in bringing farmers and veterinary surgeons closer together in the common effort of disease control and raising healthy livestock. Without the foresight, untiring energy, fighting spirit and unbounding faith of S.-B. it is difficult to predict what might have happened. The country owes much to him, and those of us who were associated with him in those critical days salute him in the name of the country for the stand he took, for the lead he gave others, and for the noble work he did for the veterinary profession and the agricultural industry.

What of the man himself? Each of us has individual assets and faults. S.-B., like all of us, had both: but the assets far outstripped his faults. He was an inspiration to those who followed his lead—in fact, it was impossible to fail to follow his lead, so energetic, so convincing, so happy was he in all he did. His honesty of purpose was outstanding: nothing was too much trouble to attain an objective in which he was interested. Once a decision was made, its attainment came first. Those early days and nights in the evolving of the Panel Scheme will for ever remain a cherished memory. The keynote was hard work, long hours and exacting details. Led by S.-B., the scheme gradually evolved, and additions were made to the group—additions who were experts in their subjects. The scope of the plan was extended, and, finally, the Scheme for the Control of Diseases of Dairy Cattle was born.

It may be that to some the scheme was a failure in that it was not widely taken up either by veterinary surgeons or by farmers. Be that as it may, the scheme fulfilled its main objective: not only did it bring the veterinary surgeon and the farmer closer together, it educated the veterinary surgeon. But for the scheme it is doubtful, for example, if infertility control and research would have progressed to its present state.

Our thoughts go out at this time to that charming, indefatigable lady—Mrs. Steele-Bodger. We have praised the man, and rightly so, but without his lady it is difficult to forecast how we would have fared in our work in those early war days. It is often said that without their ladies veterinary surgeons in practice would be lost. Never was a truer remark made than in the case of S.-B. Never can we forget all she did at Tamworth and elsewhere to make us happy and comfortable, to spur us on when we flagged through sheer fatigue, and to order our lives on these brief but important visits.

We could go on and on recounting the many incidents in our association with S.-B. Suffice it that we end this appreciation by saying the country, nay, the world, has lost a great veterinarian and a great man. May we who are left to carry on keep his memory ever fresh and continue to bear the torch which he lit and kept alight, to the benefit of this noble profession in the service of which he died.

NOTICES

NEW PREPARATION

Coccidiosis in Poultry

THE introduction of a new poultry product—"Nefco" nitrofurazone—which is administered by simply mixing with dry mash, is announced.

Recent British research shows that "Nefco" is effective in extremely small doses, which enables treatment to be carried out for as little as one penny per chick, and also that it allows natural immunity to develop with safety and does not affect the chicks' rate of growth.

"Nefco" is issued in cartons of approximately $3\frac{1}{2}$ oz. (3s. 6d. each) and 14 oz. (12s. each). Leaflets giving further information are available from the Veterinary Department, A. J. White, Ltd., Coldharbour Lane, London, S.E.5.

Lancashire Raises £4,000 For Animal Health Trust

AT the second annual general meeting of the Lancashire County Committee of the Animal Health Trust, held in Preston on February 5, it was announced that more than £4,000 had been raised in Lancashire to help the Trust's funds.

Dr. W. R. Wooldridge, M.Sc., M.R.C.V.S., F.R.I.C., Scientific Director and Chairman of Council of the Trust, briefly reviewed the progress of scientific activities during the past year.

The Earl Peel, President of the Lancashire County Committee, presided.

Publishers' Notices

THE BRITISH VETERINARY JOURNAL, with which is incorporated THE VETERINARY JOURNAL, is published monthly, and copy for advertisements should be in the hands of the advertisement manager not later than the 20th of the preceeding month, if proof is required. Tel.: Temple Bar 3386.

Letters for the Journal, literary contributions, reports, notices, books for review, exchanges, new instruments or materials, and all matter for publication (except advertisements) should be addressed to the Editor.

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